

SEQUENCE LISTING

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Friedrich Goetz
Rolf-Guenther Werner

<120> Methods for Large Scale Production of Recombinant
DNA-Derived tPA or K2S Molecules

<130> 0652.2190001

<150> 60/268,574

<151> 2001-02-15

<150> GB 0027779.8

<151> 2000-11-14

<160> 25

<170> PatentIn Ver. 2.1

<210> 1

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: coding
sequence of N-terminal part of K2S protein

<400> 1

tctgagggaa acagtgc

18

<210> 2

<211> 1128

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: coding
sequence for OmpA-K2S fusion protein

<400> 2

atgaaaaaga	cagctatcgc	gattgcagtg	gcactggctg	gtttcgctac	cgtggcccag	60
gcggcctctg	agggaaacag	tgactgctac	tttggaatg	ggtcagccta	ccgtggcacg	120
cacagcctca	ccgagtcggg	tgccctcctgc	ctcccgtgga	attccatgat	cctgataggc	180
aaggtttaca	cagcacagaa	ccccagtgcc	caggcactgg	gcctgggcaa	acataattac	240
tgccggaatc	ctgatgggga	tgccaagccc	tggtgccacg	tgctgaagaa	ccgcaggctg	300
acgtgggagt	actgtgatgt	gccctcctgc	tccacctgcg	gcctgagaca	gtacagccag	360
cctcagtttc	gcatacaaagg	agggtctctc	gccgacatcg	cctcccaccc	ctggcaggct	420
gccatctttg	ccaagcacag	gaggtcgccc	ggagagcggt	tcctgtgcgg	gggcatactc	480
atcagctcct	gctggattct	ctctgccgcc	cactgcttcc	aggagagggt	tcgcgcccac	540
cacctgacgg	tgatcttggg	cagaacatac	cgggtggtcc	ctggcgagga	ggagcagaaa	600
tttgaagtgc	aaaaatacat	tgtccataag	gaattcgatg	atgacactta	cgacaatgac	660
attgcgctgc	tcagagtgaa	atcggattcg	tcccgcgtgtg	cccaggagag	cagcgtggtc	720
cgactgtgtg	gccttccccc	ggcggacctg	cagctgccgg	actggacgga	gtgtgagctc	780
tccggctacg	gcaagcatga	ggccttgtct	cctttctatt	cggagcggtc	gaaggaggct	840
catgtcagac	tgtacccatc	cagccgctgc	acatcacaac	atttacttaa	cagaacagtc	900

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<210> 3
<211> 66
<212> DNA
<213> Escherichia coli
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<210> 4
<211> 1065
<212> DNA
<213> Artificial Sequence
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<400> 4						
tctgagggaa	acagtgactg	ctacttttggg	aatgggtcag	cctaccgtgg	cacgcacagc	60
ctcaccgagt	cgggtgcctc	ctgcctcccg	tgggaattcca	tgatcctgat	aggcaaggtt	120
tacacagcac	agaaccccag	tgcccaggca	ctgggcctgg	gcaaacataa	ttactgccgg	180
aatcctgatg	gggatgccaa	gccctgggtg	cacgtgctga	agaaccgcag	gctgcagtgg	240
gagtactgtg	atgtgcccctc	ctgtctccacc	tgcggcctga	gacagtcacg	ccagcctcag	300
tttcgcatca	aaggagggct	cttcgcgcag	atcgccctccc	acccttggca	ggctgccatc	360
tttgccaagc	acaggagggtc	gcccgagag	cggttcctgt	gcggggggcat	actcatcagc	420
tcctgctgga	ttctctctgc	cgcccactgc	ttccaggaga	ggtttccgcc	ccaccacctg	480
acggtgatct	tgggcagaac	ataccgggtg	gtccctggcg	aggaggagca	gaaatttgaa	540
gtcgaaaaat	acattgtcca	taaggaattc	gatgatgaca	cttacgcaca	tgacattgcg	600
ctgtgcagc	tgaattcgga	ttcgtcccgc	tgtgcccagg	agagcagcgt	ggtccgcact	660
gtgtgccttc	ccccggcgga	cctgcagctg	cgggactgga	cggagtgtga	gctctccggc	720
tacggcaagc	atgaggcctt	gtctcctttc	tattcggagc	ggctgaagga	ggctcatgtc	780
agactgtacc	catccagccg	ctgcacatca	caacatttac	ttaacagaac	agtcaccgcg	840
aacatgctgt	gtgctggaga	cactcggagc	ggcgggcccc	aggcaaactt	gcacgcgcgc	900
tgccaggggc	attcggggag	ccccctgggt	tgtctgaagc	atggccgcgcat	gacttttggtg	960
ggcatcatca	gctggggcct	gggtctgtga	cagaaggatg	tccggggtgt	gtacacaaag	1020
gttaccaact	acctagactg	gattcgtgac	aacatgcgac	cgtga		1065

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<210> 5
<211> 1128
<212> DNA
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: coding
sequence for OmpA-K2S fusion protein

<400> 5						
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gcggcctctg	agggaaacag	tgactgctac	tttgggaatg	ggtcagccta	ccgtggcacg	120
cacagcctca	ccgagtcggg	tgccctctgc	ctcccgtgga	attccatgat	cctgataggc	180
aagggtttaca	cagcacagaa	ccccagtgcc	caggcactgg	gcctgggcaa	acataattac	240
tgccggaatc	ctgatgggga	tgccaagccc	tggtgccacg	tgctgaagaa	ccgcaggctg	300
acgtgggagt	actgtgatgt	gccctcctgc	tcacactgcg	gcctgaagaca	gtacagccag	360

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cctcagtttc gcatcaaagg agggctcttc gccgacatcg cctcccaccc ctggcaggct 420
gccatctttg ccaagcacag gaggtcgccc ggagagcggg tctgtgctgg gggcatactc 480
atcagctcct gctggattct ctctgccgcc cactgcttcc aggagaggtt tccgccccac 540
cacctgacgg tgatcttggg cagaacatac cgggtgggtc ctggcgagga ggagcagaaa 600
tttgaagtcg aaaaatacat tgtccataag gaattcgatg atgacactta cgacaatgac 660
attgcgctgc tgcagctgaa atcggattcg tcccgtgtg cccaggagag cagcgtggtc 720
cgactgtgt gccttcccc ggcgacactg cagctgcggg actggacgga gtgtgagctc 780
tccggctacg gcaagcatga ggcttgtct cctttctatt cggagcggct gaaggaggct 840
catgtcagac tgtacccatc cagccgtgc acatcacaac attacttaa cagaacagtc 900
accgacaaca tgctgtgtgc tggagacact cggagcggcg ggccccaggc aaacttgac 960
gacgcctgcc agggcgattc gggaggcccc ctggtgtgtc tgaacgatgg ccgcatgact 1020
ttggtgggca tcatcagctg gggcctgggc tgtggacaga aggatgtccc ggtgtgttac 1080
acaaagggta ccaactacct agactggatt cgtgacaaca tgcgaccg 1128
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<210> 6
 <211> 66
 <212> DNA
 <213> Escherichia coli

<400> 6
 atgaaaaaga cagctatcgc gattgcagtg gcaactggctg gtttcgctac cgtggcccag 60
 gcggcc 66

<210> 7
 <211> 1065
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: coding
 sequence for K2S protein

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<400> 7
tctgagggaa acagtgactg ctactttggg aatgggtcag cctaccgtgg cacgcacagc 60
ctcaccgagt cgggtgcctc ctgcctccc tggaattcca tgatcctgat aggcaaggtt 120
tacacagcac agaaccccag tgcccaggca ctgggcctgg gcaaacataa ttactgccgg 180
aatcctgatg gggatgccaa gccctgggtc cactgctga agaaccgcag gctgacgtgg 240
gagtactgtg atgtgccctc ctgctccacc tgcggcctga gacagtacag ccagcctcag 300
tttcgcatca aaggagggtc cttcgccgac atcgccctcc acccctggca ggctgccatc 360
tttgccaagc acaggagggtc gcccggagag cggttcctgt gcgggggcat actcatcagc 420
tctgtctgga ttctctctgc cgcccactgc ttccaggaga ggtttccgcc ccaccacctg 480
acggtgatct tgggcagaac ataccgggtg gtccctggcg aggaggagca gaaatttgaa 540
gtcgaaaaat acattgtcca taaggaattc gatgatgaca cttacgacaa tgacattgag 600
ctgctgcagc tgaaatcgga ttctgccgc tgtgcccagg agagcagcgt ggtccgcact 660
gtgtgccttc ccccgccgga cctgcagctg ccggactgga cggagtgtga gctctccggc 720
tacggcaagc atgaggcctt gtctcctttc tattcggagc ggctgaagga ggctcatgtc 780
agactgtacc catccagccg ctgcacatca caacatttac ttaacagAAC agtcaccgac 840
aacatgctgt gtgctggaga cactcggagc ggccggcccc aggcaaactt gcacgacgcc 900
tgccagggcg attcggggag cccctgggtg tgtctgaacg atggccgcat gactttgggtg 960
ggcatcatca gctggggcct gggctgtgga cagaaggatg tcccgggtgt gtacacaaag 1020
gttaccact acctagactg gattcgtgac aacatgcgac cgtga 1065
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<210> 8
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: OmpA-K2S

<400>	8														
Met	Lys	Lys	Thr	Ala	Ile	Ala	Ile	Ala	Val	Ala	Leu	Ala	Gly	Phe	Ala
1				5					10					15	
Thr	Val	Ala	Gln	Ala	Ala	Ser	Glu	Gly	Asn	Ser	Asp	Cys	Tyr	Phe	Gly
			20					25					30		
Asn	Gly	Ser	Ala	Tyr	Arg	Gly	Thr	His	Ser	Leu	Thr	Glu	Ser	Gly	Ala
		35					40					45			
Ser	Cys	Leu	Pro	Trp	Asn	Ser	Met	Ile	Leu	Ile	Gly	Lys	Val	Tyr	Thr
	50					55					60				
Ala	Gln	Asn	Pro	Ser	Ala	Gln	Ala	Leu	Gly	Leu	Gly	Lys	His	Asn	Tyr
65					70					75					80
Cys	Arg	Asn	Pro	Asp	Gly	Asp	Ala	Lys	Pro	Trp	Cys	His	Val	Leu	Lys
				85					90					95	
Asn	Arg	Arg	Leu	Thr	Trp	Glu	Tyr	Cys	Asp	Val	Pro	Ser	Cys	Ser	Thr
			100					105					110		
Cys	Gly	Leu	Arg	Gln	Tyr	Ser	Gln	Pro	Gln	Phe	Arg	Ile	Lys	Gly	Gly
		115					120					125			
Leu	Phe	Ala	Asp	Ile	Ala	Ser	His	Pro	Trp	Gln	Ala	Ala	Ile	Phe	Ala
	130					135					140				
Lys	His	Arg	Arg	Ser	Pro	Gly	Glu	Arg	Phe	Leu	Cys	Gly	Gly	Ile	Leu
145					150					155					160
Ile	Ser	Ser	Cys	Trp	Ile	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Glu	Arg
				165					170					175	
Phe	Pro	Pro	His	His	Leu	Thr	Val	Ile	Leu	Gly	Arg	Thr	Tyr	Arg	Val
			180					185					190		
Val	Pro	Gly	Glu	Glu	Glu	Gln	Lys	Phe	Glu	Val	Glu	Lys	Tyr	Ile	Val
		195					200					205			
His	Lys	Glu	Phe	Asp	Asp	Asp	Thr	Tyr	Asp	Asn	Asp	Ile	Ala	Leu	Leu
	210					215					220				
Gln	Leu	Lys	Ser	Asp	Ser	Ser	Arg	Cys	Ala	Gln	Glu	Ser	Ser	Val	Val
225					230					235					240
Arg	Thr	Val	Cys	Leu	Pro	Pro	Ala	Asp	Leu	Gln	Leu	Pro	Asp	Trp	Thr
				245					250					255	
Glu	Cys	Glu	Leu	Ser	Gly	Tyr	Gly	Lys	His	Glu	Ala	Leu	Ser	Pro	Phe
			260					265					270		
Tyr	Ser	Glu	Arg	Leu	Lys	Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser
		275					280					285			
Arg	Cys	Thr	Ser	Gln	His	Leu	Leu	Asn	Arg	Thr	Val	Thr	Asp	Asn	Met
	290					295					300				
Leu	Cys	Ala	Gly	Asp	Thr	Arg	Ser	Gly	Gly	Pro	Gln	Ala	Asn	Leu	His
305					310					315					320

Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly
50 55 60

Asp	Ala	Lys	Pro	Trp	Cys	His	Val	Leu	Lys	Asn	Arg	Arg	Leu	Thr	Trp
65					70					75					80
Glu	Tyr	Cys	Asp	Val	Pro	Ser	Cys	Ser	Thr	Cys	Gly	Leu	Arg	Gln	Tyr
				85					90					95	
Ser	Gln	Pro	Gln	Phe	Arg	Ile	Lys	Gly	Gly	Leu	Phe	Ala	Asp	Ile	Ala
			100					105					110		
Ser	His	Pro	Trp	Gln	Ala	Ala	Ile	Phe	Ala	Lys	His	Arg	Arg	Ser	Pro
		115					120					125			
Gly	Glu	Arg	Phe	Leu	Cys	Gly	Gly	Ile	Leu	Ile	Ser	Ser	Cys	Trp	Ile
	130					135					140				
Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Glu	Arg	Phe	Pro	Pro	His	His	Leu
145					150					155					160
Thr	Val	Ile	Leu	Gly	Arg	Thr	Tyr	Arg	Val	Val	Pro	Gly	Glu	Glu	Glu
				165					170					175	
Gln	Lys	Phe	Glu	Val	Glu	Lys	Tyr	Ile	Val	His	Lys	Glu	Phe	Asp	Asp
			180					185					190		
Asp	Thr	Tyr	Asp	Asn	Asp	Ile	Ala	Leu	Leu	Gln	Leu	Lys	Ser	Asp	Ser
		195					200					205			
Ser	Arg	Cys	Ala	Gln	Glu	Ser	Ser	Val	Val	Arg	Thr	Val	Cys	Leu	Pro
	210					215					220				
Pro	Ala	Asp	Leu	Gln	Leu	Pro	Asp	Trp	Thr	Glu	Cys	Glu	Leu	Ser	Gly
225					230					235					240
Tyr	Gly	Lys	His	Glu	Ala	Leu	Ser	Pro	Phe	Tyr	Ser	Glu	Arg	Leu	Lys
				245					250					255	
Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg	Cys	Thr	Ser	Gln	His
			260					265					270		
Leu	Leu	Asn	Arg	Thr	Val	Thr	Asp	Asn	Met	Leu	Cys	Ala	Gly	Asp	Thr
		275					280					285			
Arg	Ser	Gly	Gly	Pro	Gln	Ala	Asn	Leu	His	Asp	Ala	Cys	Gln	Gly	Asp
	290					295					300				
Ser	Gly	Gly	Pro	Leu	Val	Cys	Leu	Asn	Asp	Gly	Arg	Met	Thr	Leu	Val
305					310					315					320
Gly	Ile	Ile	Ser	Trp	Gly	Leu	Gly	Cys	Gly	Gln	Lys	Asp	Val	Pro	Gly
				325					330					335	
Val	Tyr	Thr	Lys	Val	Thr	Asn	Tyr	Leu	Asp	Trp	Ile	Arg	Asp	Asn	Met
			340					345					350		

Arg Pro

<210> 12
 <211> 331
 <212> PRT
 <213> Artificial Sequence

Trp = 542360

<223> Description of Artificial Sequence: K2S 197-527

Ser 1	Gly 12	Ala	Ser	Cys 5	Leu	Pro	Trp	Asn	Ser 10	Met	Ile	Leu	Ile	Gly 15	Lys
Val	Tyr	Thr	Ala 20	Gln	Asn	Pro	Ser	Ala 25	Gln	Ala	Leu	Gly	Leu 30	Gly	Lys
His	Asn	Tyr 35	Cys	Arg	Asn	Pro	Asp 40	Gly	Asp	Ala	Lys	Pro 45	Trp	Cys	His
Val	Leu 50	Lys	Asn	Arg	Arg	Leu 55	Thr	Trp	Glu	Tyr	Cys 60	Asp	Val	Pro	Ser
Cys 65	Ser	Thr	Cys	Gly	Leu 70	Arg	Gln	Tyr	Ser	Gln 75	Pro	Gln	Phe	Arg	Ile 80
Lys	Gly	Gly	Leu	Phe 85	Ala	Asp	Ile	Ala	Ser 90	His	Pro	Trp	Gln	Ala 95	Ala
Ile	Phe	Ala	Lys 100	His	Arg	Arg	Ser	Pro 105	Gly	Glu	Arg	Phe	Leu 110	Cys	Gly
Gly	Ile	Leu 115	Ile	Ser	Ser	Cys	Trp 120	Ile	Leu	Ser	Ala	Ala 125	His	Cys	Phe
Gln	Glu 130	Arg	Phe	Pro	Pro	His 135	His	Leu	Thr	Val	Ile 140	Leu	Gly	Arg	Thr
Tyr 145	Arg	Val	Val	Pro	Gly 150	Glu	Glu	Glu	Gln	Lys 155	Phe	Glu	Val	Glu	Lys 160
Tyr	Ile	Val	His	Lys 165	Glu	Phe	Asp	Asp	Asp 170	Thr	Tyr	Asp	Asn	Asp 175	Ile
Ala	Leu	Leu	Gln 180	Leu	Lys	Ser	Asp	Ser 185	Ser	Arg	Cys	Ala	Gln 190	Glu	Ser
Ser	Val	Val 195	Arg	Thr	Val	Cys	Leu 200	Pro	Pro	Ala	Asp	Leu 205	Gln	Leu	Pro
Asp	Trp 210	Thr	Glu	Cys	Glu	Leu 215	Ser	Gly	Tyr	Gly	Lys 220	His	Glu	Ala	Leu
Ser 225	Pro	Phe	Tyr	Ser	Glu 230	Arg	Leu	Lys	Glu	Ala 235	His	Val	Arg	Leu	Tyr 240
Pro	Ser	Ser	Arg	Cys 245	Thr	Ser	Gln	His	Leu 250	Leu	Asn	Arg	Thr	Val 255	Thr
Asp	Asn	Met	Leu 260	Cys	Ala	Gly	Asp	Thr 265	Arg	Ser	Gly	Gly	Pro 270	Gln	Ala
Asn	Leu	His 275	Asp	Ala	Cys	Gln	Gly 280	Asp	Ser	Gly	Gly	Pro 285	Leu	Val	Cys
Leu	Asn 290	Asp	Gly	Arg	Met	Thr 295	Leu	Val	Gly	Ile	Ile 300	Ser	Trp	Gly	Leu
Gly	Cys	Gly	Gln	Lys	Asp	Val	Pro	Gly	Val	Tyr	Thr	Lys	Val	Thr	Asn

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<210> 13
<211> 339
<212> PRT
<213> Artificial Sequence
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<400>	13														
Ser 1	Glu	Gly	Asn	Ser 5	Leu	Thr	Glu	Ser	Gly 10	Ala	Ser	Cys	Leu	Pro 15	Trp
Asn	Ser	Met	Ile 20	Leu	Ile	Gly	Lys 25	Val	Tyr	Thr	Ala	Gln 30	Asn	Pro	Ser
Ala	Gln	Ala 35	Leu	Gly	Leu	Gly	Lys 40	His	Asn	Tyr	Cys	Arg 45	Asn	Pro	Asp
Gly	Asp 50	Ala	Lys	Pro	Trp	Cys 55	His	Val	Leu	Lys	Asn 60	Arg	Arg	Leu	Thr
Trp 65	Glu	Tyr	Cys	Asp	Val 70	Pro	Ser	Cys	Ser	Thr 75	Cys	Gly	Leu	Arg	Gln 80
Tyr	Ser	Gln	Pro	Gln 85	Phe	Arg	Ile	Lys	Gly 90	Gly	Leu	Phe	Ala	Asp 95	Ile
Ala	Ser	His	Pro 100	Trp	Gln	Ala	Ala 105	Ile	Phe	Ala	Lys	His 110	Arg	Arg	Ser
Pro	Gly	Glu 115	Arg	Phe	Leu	Cys	Gly 120	Gly	Ile	Leu	Ile	Ser 125	Ser	Cys	Trp
Ile 130	Leu	Ser	Ala	Ala	His	Cys 135	Phe	Gln	Glu	Arg	Phe 140	Pro	Pro	His	His
Leu 145	Thr	Val	Ile	Leu	Gly 150	Arg	Thr	Tyr	Arg	Val 155	Val	Pro	Gly	Glu	Glu 160
Glu	Gln	Lys	Phe 165	Glu	Val	Glu	Lys	Tyr	Ile 170	Val	His	Lys	Glu	Phe 175	Asp
Asp	Asp	Thr	Tyr 180	Asp	Asn	Asp	Ile	Ala 185	Leu	Leu	Gln	Leu	Lys 190	Ser	Asp
Ser	Ser	Arg 195	Cys	Ala	Gln	Glu	Ser 200	Ser	Val	Val	Arg	Thr 205	Val	Cys	Leu
Pro	Pro 210	Ala	Asp	Leu	Gln	Leu 215	Pro	Asp	Trp	Thr	Glu 220	Cys	Glu	Leu	Ser
Gly 225	Tyr	Gly	Lys	His	Glu 230	Ala	Leu	Ser	Pro	Phe 235	Tyr	Ser	Glu	Arg	Leu 240
Lys	Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg	Cys	Thr	Ser	Gln


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<210> 14
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 193-527,
      modified

<400> 14
Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
 1          5          10
Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
          20          25          30
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
          35          40          45
Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
          50          55          60
Asp Val Pro Ser Ser Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
 65          70          75          80
Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
          85          90          95
Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
          100          105          110
Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
          115          120          125
Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
          130          135          140
Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
145          150          155          160
Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr

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175

Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
325 330 335

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<210> 15
<211> 343
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: K2S 191-527,
modified

<400> 15
Ser Glu Gly Asn Ser Asp Thr His Ser Leu Thr Glu Ser Gly Ala Ser
1 5 10 15

Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala
20 25 30

Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys
35 40 45

Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn
50 55 60

Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys
65 70 75 80

Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu
85 90 95

Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys

100					105					110					
His	Arg	Arg	Ser	Pro	Gly	Glu	Arg	Phe	Leu	Cys	Gly	Gly	Ile	Leu	Ile
		115					120					125			
Ser	Ser	Cys	Trp	Ile	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Glu	Arg	Phe
	130					135					140				
Pro	Pro	His	His	Leu	Thr	Val	Ile	Leu	Gly	Arg	Thr	Tyr	Arg	Val	Val
145					150					155					160
Pro	Gly	Glu	Glu	Glu	Gln	Lys	Phe	Glu	Val	Glu	Lys	Tyr	Ile	Val	His
				165					170					175	
Lys	Glu	Phe	Asp	Asp	Asp	Thr	Tyr	Asp	Asn	Asp	Ile	Ala	Leu	Leu	Gln
			180					185					190		
Leu	Lys	Ser	Asp	Ser	Ser	Arg	Cys	Ala	Gln	Glu	Ser	Ser	Val	Val	Arg
		195					200					205			
Thr	Val	Cys	Leu	Pro	Pro	Ala	Asp	Leu	Gln	Leu	Pro	Asp	Trp	Thr	Glu
	210					215					220				
Cys	Glu	Leu	Ser	Gly	Tyr	Gly	Lys	His	Glu	Ala	Leu	Ser	Pro	Phe	Tyr
225					230					235					240
Ser	Glu	Arg	Leu	Lys	Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg
				245					250					255	
Cys	Thr	Ser	Gln	His	Leu	Leu	Asn	Arg	Thr	Val	Thr	Asp	Asn	Met	Leu
			260					265					270		
Cys	Ala	Gly	Asp	Thr	Arg	Ser	Gly	Gly	Pro	Gln	Ala	Asn	Leu	His	Asp
		275					280					285			
Ala	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Leu	Asn	Asp	Gly
	290					295					300				
Arg	Met	Thr	Leu	Val	Gly	Ile	Ile	Ser	Trp	Gly	Leu	Gly	Cys	Gly	Gln
305					310					315					320
Lys	Asp	Val	Pro	Gly	Val	Tyr	Thr	Lys	Val	Thr	Asn	Tyr	Leu	Asp	Trp
				325					330					335	
Ile	Arg	Asp	Asn	Met	Arg	Pro									
			340												

<210> 16
 <211> 343
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: K2S 191-527,
 modified

<400> 16
 Ser Glu Gly Asn Ser Asp Thr His Ser Leu Thr Glu Ser Gly Ala Ser
 1 5 10 15
 Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala

			20				25				30					
Gln	Asn	Pro	Ser	Ala	Gln	Ala	Leu	Gly	Leu	Gly	Lys	His	Asn	Tyr	Cys	
		35					40					45				
Arg	Asn	Pro	Asp	Gly	Asp	Ala	Lys	Pro	Trp	Cys	His	Val	Leu	Lys	Asn	
		50					55					60				
Arg	Arg	Leu	Thr	Trp	Glu	Tyr	Cys	Asp	Val	Pro	Ser	Ser	Ser	Thr	Cys	
		65			70					75			80			
Gly	Leu	Arg	Gln	Tyr	Ser	Gln	Pro	Gln	Phe	Arg	Ile	Lys	Gly	Gly	Leu	
				85					90					95		
Phe	Ala	Asp	Ile	Ala	Ser	His	Pro	Trp	Gln	Ala	Ala	Ile	Phe	Ala	Lys	
				100					105					110		
His	Arg	Arg	Ser	Pro	Gly	Glu	Arg	Phe	Leu	Cys	Gly	Gly	Ile	Leu	Ile	
		115					120					125				
Ser	Ser	Cys	Trp	Ile	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Glu	Arg	Phe	
		130					135					140				
Pro	Pro	His	His	Leu	Thr	Val	Ile	Leu	Gly	Arg	Thr	Tyr	Arg	Val	Val	
		145			150					155					160	
Pro	Gly	Glu	Glu	Glu	Gln	Lys	Phe	Glu	Val	Glu	Lys	Tyr	Ile	Val	His	
				165					170					175		
Lys	Glu	Phe	Asp	Asp	Asp	Thr	Tyr	Asp	Asn	Asp	Ile	Ala	Leu	Leu	Gln	
				180					185					190		
Leu	Lys	Ser	Asp	Ser	Ser	Arg	Cys	Ala	Gln	Glu	Ser	Ser	Val	Val	Arg	
		195					200					205				
Thr	Val	Cys	Leu	Pro	Pro	Ala	Asp	Leu	Gln	Leu	Pro	Asp	Trp	Thr	Glu	
		210					215					220				
Cys	Glu	Leu	Ser	Gly	Tyr	Gly	Lys	His	Glu	Ala	Leu	Ser	Pro	Phe	Tyr	
		225			230					235					240	
Ser	Glu	Arg	Leu	Lys	Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg	
				245					250					255		
Cys	Thr	Ser	Gln	His	Leu	Leu	Asn	Arg	Thr	Val	Thr	Asp	Asn	Met	Leu	
				260					265					270		
Cys	Ala	Gly	Asp	Thr	Arg	Ser	Gly	Gly	Pro	Gln	Ala	Asn	Leu	His	Asp	
		275					280					285				
Ala	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Leu	Asn	Asp	Gly	
		290					295					300				
Arg	Met	Thr	Leu	Val	Gly	Ile	Ile	Ser	Trp	Gly	Leu	Gly	Cys	Gly	Gln	
		305			310					315					320	
Lys	Asp	Val	Pro	Gly	Val	Tyr	Thr	Lys	Val	Thr	Asn	Tyr	Leu	Asp	Trp	
				325					330					335		
Ile	Arg	Asp	Asn	Met	Arg	Pro										
				340												

<220>
<223> Description of Artificial Sequence: K2S 220-527

<400>	17														
Ser	Ala	Gln	Ala	Leu	Gly	Leu	Gly	Lys	His	Asn	Tyr	Cys	Arg	Asn	Pro
1				5					10					15	
Asp	Gly	Asp	Ala	Lys	Pro	Trp	Cys	His	Val	Leu	Lys	Asn	Arg	Arg	Leu
			20					25					30		
Thr	Trp	Glu	Tyr	Cys	Asp	Val	Pro	Ser	Cys	Ser	Thr	Cys	Gly	Leu	Arg
		35					40					45			
Gln	Tyr	Ser	Gln	Pro	Gln	Phe	Arg	Ile	Lys	Gly	Gly	Leu	Phe	Ala	Asp
	50					55					60				
Ile	Ala	Ser	His	Pro	Trp	Gln	Ala	Ala	Ile	Phe	Ala	Lys	His	Arg	Arg
65					70					75					80
Ser	Pro	Gly	Glu	Arg	Phe	Leu	Cys	Gly	Gly	Ile	Leu	Ile	Ser	Ser	Cys
				85					90					95	
Trp	Ile	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Glu	Arg	Phe	Pro	Pro	His
			100					105					110		
His	Leu	Thr	Val	Ile	Leu	Gly	Arg	Thr	Tyr	Arg	Val	Val	Pro	Gly	Glu
		115					120					125			
Glu	Glu	Gln	Lys	Phe	Glu	Val	Glu	Lys	Tyr	Ile	Val	His	Lys	Glu	Phe
	130					135					140				
Asp	Asp	Asp	Thr	Tyr	Asp	Asn	Asp	Ile	Ala	Leu	Leu	Gln	Leu	Lys	Ser
145					150					155					160
Asp	Ser	Ser	Arg	Cys	Ala	Gln	Glu	Ser	Ser	Val	Val	Arg	Thr	Val	Cys
				165					170					175	
Leu	Pro	Pro	Ala	Asp	Leu	Gln	Leu	Pro	Asp	Trp	Thr	Glu	Cys	Glu	Leu
			180					185					190		
Ser	Gly	Tyr	Gly	Lys	His	Glu	Ala	Leu	Ser	Pro	Phe	Tyr	Ser	Glu	Arg
		195					200					205			
Leu	Lys	Glu	Ala	His	Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg	Cys	Thr	Ser
	210					215					220				
Gln	His	Leu	Leu	Asn	Arg	Thr	Val	Thr	Asp	Asn	Met	Leu	Cys	Ala	Gly
225					230					235					240
Asp	Thr	Arg	Ser	Gly	Gly	Pro	Gln	Ala	Asn	Leu	His	Asp	Ala	Cys	Gln
				245					250					255	
Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Leu	Asn	Asp	Gly	Arg	Met	Thr
			260					265					270		
Leu	Val	Gly	Ile	Ile	Ser	Trp	Gly	Leu	Gly	Cys	Gly	Gln	Lys	Asp	Val
		275					280					285			

Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp
290 295 300

Asn Met Arg Pro
305

<210> 18
<211> 268
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 260-527

<400> 18
Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg
1 5 10 15
Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala
20 25 30
Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys
35 40 45
Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys
50 55 60
Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg
65 70 75 80
Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu
85 90 95
Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp
100 105 110
Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu
115 120 125
Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu
130 135 140
Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala
145 150 155 160
Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu
165 170 175
Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val
180 185 190
Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln
195 200 205
Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
210 215 220
Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly
225 230 235 240
Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr

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255

<400>	19														
Ser	Tyr	Gln	Val	Ile	Cys	Arg	Asp	Glu	Lys	Thr	Gln	Met	Ile	Tyr	Gln
1				5					10					15	
Gln	His	Gln	Ser	Trp	Leu	Arg	Pro	Val	Leu	Arg	Ser	Asn	Arg	Val	Glu
			20					25					30		
Tyr	Cys	Trp	Cys	Asn	Ser	Gly	Arg	Ala	Gln	Cys	His	Ser	Val	Pro	Val
		35					40					45			
Lys	Ser	Cys	Ser	Glu	Pro	Arg	Cys	Phe	Asn	Gly	Gly	Thr	Cys	Gln	Gln
	50					55					60				
Ala	Leu	Tyr	Phe	Ser	Asp	Phe	Val	Cys	Gln	Cys	Pro	Glu	Gly	Phe	Ala
65					70					75					80
Gly	Lys	Cys	Cys	Glu	Ile	Asp	Thr	Arg	Ala	Thr	Cys	Tyr	Glu	Asp	Gln
				85					90					95	
Gly	Ile	Ser	Tyr	Arg	Gly	Thr	Trp	Ser	Thr	Ala	Glu	Ser	Gly	Ala	Glu
			100					105					110		
Cys	Thr	Asn	Trp	Asn	Ser	Ser	Ala	Leu	Ala	Gln	Lys	Pro	Tyr	Ser	Gly
		115					120					125			
Arg	Arg	Pro	Asp	Ala	Ile	Arg	Leu	Gly	Leu	Gly	Asn	His	Asn	Tyr	Cys
	130					135					140				
Arg	Asn	Pro	Asp	Arg	Asp	Ser	Lys	Pro	Trp	Cys	Tyr	Val	Phe	Lys	Ala
145					150					155					160
Gly	Lys	Tyr	Ser	Ser	Glu	Phe	Cys	Ser	Thr	Pro	Ala	Cys	Ser	Glu	Gly
				165					170					175	
Asn	Ser	Asp	Cys	Tyr	Phe	Gly	Asn	Gly	Ser	Ala	Tyr	Arg	Gly	Thr	His
			180					185					190		
Ser	Leu	Thr	Glu	Ser	Gly	Ala	Ser	Cys	Leu	Pro	Trp	Asn	Ser	Met	Ile
		195					200					205			
Leu	Ile	Gly	Lys	Val	Tyr	Thr	Ala	Gln	Asn	Pro	Ser	Ala	Gln	Ala	Leu
	210					215					220				
Gly	Leu	Gly	Lys	His	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Gly	Asp	Ala	Lys
225					230					235					240
Pro	Trp	Cys	His	Val	Leu	Lys	Asn	Arg	Arg	Leu	Thr	Trp	Glu	Tyr	Cys
				245					250					255	
Asp	Val	Pro	Ser	Cys	Ser	Thr	Cys	Gly	Leu	Arg	Gln	Tyr	Ser	Gln	Pro
			260					265					270		

Gln	Phe	Arg	Ile	Lys	Gly	Gly	Leu	Phe	Ala	Asp	Ile	Ala	Ser	His	Pro
		275					280					285			
Trp	Gln	Ala	Ala	Ile	Phe	Ala	Lys	His	Arg	Arg	Ser	Pro	Gly	Glu	Arg
	290					295					300				
Phe	Leu	Cys	Gly	Gly	Ile	Leu	Ile	Ser	Ser	Cys	Trp	Ile	Leu	Ser	Ala
305					310					315					320
Ala	His	Cys	Phe	Gln	Glu	Arg	Phe	Pro	Pro	His	His	Leu	Thr	Val	Ile
				325					330					335	
Leu	Gly	Arg	Thr	Tyr	Arg	Val	Val	Pro	Gly	Glu	Glu	Glu	Gln	Lys	Phe
			340					345					350		
Glu	Val	Glu	Lys	Tyr	Ile	Val	His	Lys	Glu	Phe	Asp	Asp	Asp	Thr	Tyr
		355					360					365			
Asp	Asn	Asp	Ile	Ala	Leu	Leu	Gln	Leu	Lys	Ser	Asp	Ser	Ser	Arg	Cys
	370					375					380				
Ala	Gln	Glu	Ser	Ser	Val	Val	Arg	Thr	Val	Cys	Leu	Pro	Pro	Ala	Asp
385					390					395					400
Leu	Gln	Leu	Pro	Asp	Trp	Thr	Glu	Cys	Glu	Leu	Ser	Gly	Tyr	Gly	Lys
				405					410					415	
His	Glu	Ala	Leu	Ser	Pro	Phe	Tyr	Ser	Glu	Arg	Leu	Lys	Glu	Ala	His
			420					425					430		
Val	Arg	Leu	Tyr	Pro	Ser	Ser	Arg	Cys	Thr	Ser	Gln	His	Leu	Leu	Asn
		435					440					445			
Arg	Thr	Val	Thr	Asp	Asn	Met	Leu	Cys	Ala	Gly	Asp	Thr	Arg	Ser	Gly
	450					455					460				
Gly	Pro	Gln	Ala	Asn	Leu	His	Asp	Ala	Cys	Gln	Gly	Asp	Ser	Gly	Gly
465					470					475					480
Pro	Leu	Val	Cys	Leu	Asn	Asp	Gly	Arg	Met	Thr	Leu	Val	Gly	Ile	Ile
				485					490					495	
Ser	Trp	Gly	Leu	Gly	Cys	Gly	Gln	Lys	Asp	Val	Pro	Gly	Val	Tyr	Thr
			500					505					510		
Lys	Val	Thr	Asn	Tyr	Leu	Asp	Trp	Ile	Arg	Asp	Asn	Met	Arg	Pro	
		515					520					525			

<210> 20

<211> 12

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: coding
sequence for SEGN

<400> 20

tctgagggaa ac

